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(71) Applicant (for all designated States except US): POLY-  
THERICS LIMITED [GB/GB]; 90 Fetter Lane, London  
EC4A 1JP (GB).

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(72) Inventors; and

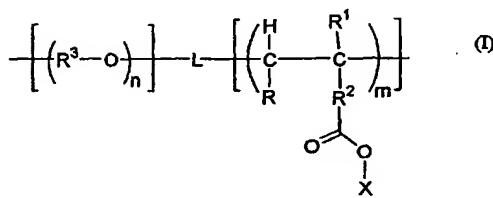
(75) Inventors/Applicants (for US only): BROCCINI, Steve  
[US/GB]; 15, Westly Wood, Welwyn Garden City, Hert-  
fordshire AL7 1QN (GB). GODWIN, Antony [GB/GB];  
159 St Peters Rise, Headley Park, Bristol BS13 7QR (GB).

(74) Agents: SCOTT, Susan, Margaret et al.; Abel & Imray,  
20 Red Lion Street, London WC1R 4PQ (GB).

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(54) Title: BLOCK COPOLYMERS



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(57) Abstract: Novel block copolymers are described, together with the production therefrom of physiologically soluble polymer therapeutics. The block copolymers have the general formula (1) wherein R is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>18</sub> alkyl, C<sub>2</sub>-C<sub>18</sub> alkenyl, C<sub>7</sub>-C<sub>18</sub> aralkyl, C<sub>7</sub>-C<sub>18</sub> alkaryl, C<sub>6</sub>-C<sub>18</sub> aryl, carboxylic acid, C<sub>2</sub>-C<sub>18</sub> alkoxy carbonyl, C<sub>2</sub>-C<sub>18</sub> alkaminocarbonyl, or any one of C<sub>1</sub>-C<sub>18</sub> alkyl, C<sub>2</sub>-C<sub>18</sub> alkenyl, C<sub>7</sub>-C<sub>18</sub> aralkyl, C<sub>7</sub>-C<sub>18</sub> alkaryl, C<sub>6</sub>-C<sub>18</sub> aryl, C<sub>2</sub>-C<sub>18</sub> alkoxy carbonyl and C<sub>2</sub>-C<sub>18</sub> alkaminocarbonyl substituted with a heteroatom within, or attached to, the carbon backbone; R<sup>1</sup> is selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>6</sub> alkyl groups; R<sup>2</sup> is a linking group; X is an electron withdrawing group; R<sup>3</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>18</sub> alkylene, C<sub>2</sub>-C<sub>18</sub> alkenylene, C<sub>7</sub>-C<sub>18</sub> aralkylene, C<sub>7</sub>-C<sub>18</sub> alarylene and C<sub>6</sub>-C<sub>18</sub> arylene; L is a divalent linker joining the blocks; and m and n are each an integer of greater than 1.

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB 02/05932A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C08F293/00 A61K31/00 C08F20/36 C08F4/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C08F C08L A61K C08G C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 18080 A (BROCCINI STEPHEN JAMES ; GODWIN ANTONY (GB); UNIV LONDON PHARMACY) 15 March 2001 (2001-03-15) cited in the application * page 18, line 9-10, 14-15 (particularly polyethylene glycol) ; page 26, line 8-9 ; claims 1-38 ; examples * page 17, line 7 -page 28, line 15 --- US 6 235 813 B1 (SILBER STEFAN ET AL) 22 May 2001 (2001-05-22) * claim 1 ; column 3, line 25 ; column 2, line 40 - column 3, line 29 ; claims 9, 2-19 ; examples * column 5, line 66 -column 6, line 57 --- -/-	1-7,11
X		1-7,11

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

## \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance  
 "E" earlier document but published on or after the International filing date  
 "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  
 "O" document referring to an oral disclosure, use, exhibition or other means  
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 "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone  
 "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.  
 "&" document member of the same patent family

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European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Hammond, A

## INTERNATIONAL SEARCH REPORT

International Application No  
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 248 839 B1 (KNEBELKAMP ARNO ET AL) 19 June 2001 (2001-06-19) * claim 1 ; column 2, line 25 - column 4, line 8 ; examples * ---	1-7,11
X	WO 01 17515 A (BROCCHINI STEVEN JAMES ;CLOCHARD MARIE CLAUDE DUBOIS (GB); UNIV L0) 15 March 2001 (2001-03-15) * claims 8, 9, 17-22, 1-16 ; page 9, line 19 - page 23, line 10 ; examples * ---	1-7,11
A	DE 31 31 848 A (GOLDSCHMIDT AG TH) 24 February 1983 (1983-02-24) abstract; claims 1-12 ---	1-7,11
A	US 6 162 882 A (MATYJASZEWSKI KRZYSZTOF ET AL) 19 December 2000 (2000-12-19) * column 1, line 25-28 ; column 2, line 65 - column 3, line 8 ; column 9, line 36-38* column 7, line 48 -column 18, line 20 ---	1-7,11
A	US 5 763 548 A (MATYJASZEWSKI KRZYSZTOF ET AL) 9 June 1998 (1998-06-09) * column 6, line 30 ; column 6, line 37 - column 31, line 45 * column 3, line 33-54 ---	1-7,11
A	DE 195 20 875 A (BASF CORP) 14 December 1995 (1995-12-14) * abstract ; claim 1 * page 2, line 58 -page 4, line 20 ---	1-7,11
A	WO 00 55218 A (CALIFORNIA INST OF TECHN) 21 September 2000 (2000-09-21) * page 2, line 19 - page 3, line 7 * page 11, line 20-22; claims 1-33 ---	1-7,11
A	US 6 174 953 B1 (HUYBRECHTS JOSEF) 16 January 2001 (2001-01-16) * claims 1-5 * column 2, line 26 -column 4, line 31 ---	1-7,11
A	US 6 124 411 A (MATYJASZEWSKI KRZYSZTOF ET AL) 26 September 2000 (2000-09-26) * claims 1-16 * the whole document ---	1-7,11
A	WO 99 39731 A (SUPRATEK PHARMA INC ;ALAKOV VALERY Y (CA); BATRAKOVA ELENA V (US);) 12 August 1999 (1999-08-12) claims 1-21 -----	1-7,11

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 02/05932

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-7, 11

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-7,11

A block copolymer comprising the unit (I) :  
-(-(R3-O)<sub>n</sub>)-L-(-(CHR-CR1(R2COOX)-)<sub>m</sub>)-...(I), wherein m, n, L, X, R, R1, R2, R3 are as described in the application claim 1.

2. Claims: 8,9,10

A further specific block copolymer related to the general block copolymer formula (I) according to any one of the proceeding claims, but wherein R2 is specifically defined as described in application claims 8-10.

3. Claim : 11

A further specific block copolymer related to the general block copolymer formula (I) according to any one of the preceding claims, but wherein R3 is specifically defined as described in claim 11.

4. Claim : 12

A further specific block copolymer related to the general block copolymer formula (I) according to claim 11, but wherein all R3 groups are the same and are preferably all 1,2-ethylene or 1,2-propylene.

5. Claims: 13,14

A further specific block copolymer related to the general block copolymer formula (I) according to any one of the preceding claims, but wherein L is specifically defined as described in claims 13,14.

6. Claim : 15

A further specific block copolymer related to the general block copolymer formula (I) according to claim 14, but wherein L comprises a CORa group, wherein Ra is specifically defined as described in claim 15.

7. Claims: 16-22

A further block copolymer comprising the structure (II) related to the general block copolymer formula (I), but

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

which comprises as the structure (II) :  
-(-(R7-O)n-)-L1-(-(CHR12-CR13(R14COZ)-)m-(-(CHR4-CR5(R6COQ)-)  
p)-... (II) , wherein the various components are as  
described in application claim 16.

8. Claims: 23-32

A process for the production of a block copolymer,  
comprising the polymerisation of ethylenically unsaturated  
monomers including a compound of structure (III) as  
described in claim 23.

9. Claim : 33

A process for the production of a block copolymer comprising  
the steps as described in claim 33, of polymerising  
ethylenically unsaturated monomers comprising a compound  
(VIII) as described in claim 33.

10. Claim : 34

A specific process related to claim 23 or claim 33, but  
wherein the ethylenically unsaturated monomer compound is  
specifically structure (XIII) as described in claim 34, and  
the initiator is specifically structure (XIV) as described  
in claim 34.

11. Claim : 35

A specific process related to claim 34, but wherein the  
copolymer is further reacted with a compound :  
H2N-Gly-Len-Phe-Gly-Doxorubicin,  
then followed by a further process step in which the product  
of the above reaction is further reacted with  
2-hydroxy-propylamine.

12. Claim : 36

A specific block copolymer related to the general block  
copolymer formula (I), but wherein the block copolymer has  
the specific structure (XII) as described in claim 36.

13. Claim : 37

A further block copolymer which is obtainable by reacting  
the block copolymer of claim 36 and a reagent selected to  
provide a pendant group comprising an aminoacyl linker or a  
cis-aconityl linker and a bioactive agent.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 02/05932

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